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H3G 1T3 (CA). **THIBAUDEAU, Karen** [FR/CA]; 4700
Bonavista Street, #407, Montreal, Quebec H3W 2L5 (CA).

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(74) Agents: **WARD, Michael, R.** et al.; Morrison & Foerster,
LLP, 755 Page Mill Road, Palo Alto, CA 94304-1018 (US).

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(71) Applicant (*for all designated States except US*): **CON-
JUCHEM, INC.** [CA/CA]; Suite 3950, Third Floor, 225
President Kennedy Avenue West, Montreal, Quebec H2X
3Y8 (CA).

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(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **BRIDON, Do-
minique, P.** [FR/CA]; 243 chemin Cote Ste-Catherine,
Outremont, Quebec H2V 2B2 (CA). **EZRIN, Alan, M.**
[US/US]; 110 Quintas Lane, Moraga, CA 94556 (US).
MILNER, Peter, G. [GB/US]; 14690 Manuella Road,
Los Altos Hills, CA 94022 (US). **HOLMES, Darren,
L.** [US/CA]; 3450 Drummond Street, Montreal, Quebec

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ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: PROTECTION OF ENDOGENOUS THERAPEUTIC PEPTIDES FROM PEPTIDASE ACTIVITY THROUGH CON-
JUGATION TO BLOOD COMPONENTS

(57) Abstract: A method for protecting a peptide from peptidase activity *in vivo*, the peptide being composed of between 2 and 50 amino acids and having a C-terminus and an N-terminus and a C-terminus amino acid and an N-terminus amino acid is described. In the first step of the method, the peptide is modified by attaching a reactive group to the C-terminus amino acid, to the N-terminus amino acid, or to an amino acid located between the N-terminus and the C-terminus, such that the modified peptide is capable of forming a covalent bond *in vivo* with a reactive functionality on a blood component. In the next step, a covalent bond is formed between the reactive group and a reactive functionality on a blood component to form a peptide-blood component conjugate, thereby protecting said peptide from peptidase activity. The final step of the method involves the analyzing of the stability of the peptide-blood component conjugate to assess the protection of the peptide from peptidase activity.

INTERNATIONAL SEARCH REPORT

International Application No

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A. CLASSIFICATION OF SUBJECT MATTER

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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, MEDLINE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 602 290 A (POULETTY PHILIPPE ;POULETTY CHRISTINE (US)) 22 June 1994 (1994-06-22) column 2, line 1 - line 22 column 8, line 25 - line 33; claims ---	1-10,12, 13,16,21
X	WO 95 10302 A (REDCCELL INC) 20 April 1995 (1995-04-20) page 18, line 10 -page 19, line 1 ---	1-10,12, 13,16,21
A	US 5 580 853 A (SYTKOWSKI ARTHUR J) 3 December 1996 (1996-12-03) column 3, line 42 -column 4, line 38 column 5, line 21 - line 4 column 7, line 38 - line 43 --- -/--	1-10,12, 13,16,21

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

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Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Fuhr, C

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 654 276 A (BARRETT RONALD W ET AL) 5 August 1997 (1997-08-05) column 3, line 28 - line 38 column 17, line 48 -column 18, line 8; claims ----	1-5
P,X	WO 99 48536 A (CONJUCHEM INC ;HOLMES DARREN L (CA); BRIDON DOMINIQUE P (CA); EZRI) 30 September 1999 (1999-09-30) claims; examples ----	1-26
P,X	WO 99 24462 A (CONJUCHEM INC ;HOLMES DARREN L (CA); BRIDON DOMINIQUE P (CA); THIB) 20 May 1999 (1999-05-20) claims; examples ----	1-26
P,A	WO 99 24075 A (CONJUCHEM INC ;HOLMES DARREN L (CA); BRIDON DOMINIQUE P (CA); HUAN) 20 May 1999 (1999-05-20) claims; examples -----	1-26

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-26 relate to an extremely large number of possible compounds and methods. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds and methods claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the general concept of the invention i.e. the method of activating pharmaceutically or biologically active peptides using maleimido- or succinimido groups; as a result the activated peptides bind to blood components like albumin which decreases susceptibility for protease degradation. The search was directed to the underlying concept. The search was not direct to retrieve compounds or conjugates falling under the scope of claims 1-5 or the examples.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0602290 A	22-06-1994	NONE	
WO 9510302 A	20-04-1995	US 5612034 A AU 693813 B AU 7955894 A CA 2172630 A EP 0793506 A JP 9503511 T US 6103233 A US 5843440 A	18-03-1997 09-07-1998 04-05-1995 20-04-1995 10-09-1997 08-04-1997 15-08-2000 01-12-1998
US 5580853 A	03-12-1996	AT 188486 T DE 69514342 D DK 751959 T EP 0751959 A ES 2143620 T PT 751959 T US 5919758 A WO 9525746 A US 6107272 A US 5747446 A	15-01-2000 10-02-2000 26-06-2000 08-01-1997 16-05-2000 30-06-2000 06-07-1999 28-09-1995 22-08-2000 05-05-1998
US 5654276 A	05-08-1997	NONE	
WO 9948536 A	30-09-1999	AU 3452799 A EP 1042003 A	18-10-1999 11-10-2000
WO 9924462 A	20-05-1999	AU 1312799 A AU 1385699 A AU 1519699 A AU 1519799 A EP 1007561 A EP 1028971 A WO 9924074 A WO 9924075 A WO 9924076 A	31-05-1999 31-05-1999 31-05-1999 31-05-1999 14-06-2000 23-08-2000 20-05-1999 20-05-1999 20-05-1999
WO 9924075 A	20-05-1999	AU 1312799 A AU 1385699 A AU 1519699 A AU 1519799 A EP 1007561 A EP 1028971 A WO 9924462 A WO 9924074 A WO 9924076 A	31-05-1999 31-05-1999 31-05-1999 31-05-1999 14-06-2000 23-08-2000 20-05-1999 20-05-1999 20-05-1999